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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/052,824	11/07/2001	Fernand Labrie	P/1259-636	4181

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EXAMINER	
JIANG, SHAOJIA A	
ART UNIT	**PAPER NUMBER**
1617	10

DATE MAILED: 06/18/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	10/052,824	LABRIE, FERNAND	
	Examin r	Art Unit	
	Shaojia A. Jiang	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 March 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28* is/are pending in the application.

4a) Of the above claim(s) *7-12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6 and 13-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

This Office Action is a response to Applicant's amendment and response filed on March 26, 2003 in Paper No. 9 wherein the instant specification has been amended as to page 77-78, Table 8, and page 27 line 21-28. Currently, claims 1-28 are pending in this application.

As indicated in the previous Office Action dated November 20, 2002 and May 21, 2002, claims 7-12 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. The claims have been examined insofar as they read on the elected specie.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 3 is rejected under 35 U.S.C. 112, second paragraph, for the use of the indefinite expressions, "an androgenic agent" in claim 3, of record in the Office Action dated November 20, 2002 and May 21, 2002.

Applicant's remarks filed on March 26, 2003 in Paper No. 9 with respect to this rejection made under 35 U.S.C. 112 second paragraph have been fully considered but they are not deemed persuasive to remove the rejection. As discussed in the previous Office Action, the expression "an androgenic agent" in claim 3 renders claim 3 indefinite as failing to clearly set forth the metes and bounds of the patent protection desired. The specification at page 22 lines 16-20 merely describes the function of "an androgenic

agent", but fails to set forth what particular androgenic agents employed in the instant invention. The particular androgenic agent, MPA, employed in Fig. 4 in the specification as Applicant asserts, is merely a single androgenic agent. Applicant also argues that "androgenic agent" is well known class of materials in the art. However, the CAFC further clearly states that "[A] written description of an invention involving a chemical genus, like a description of a chemical species, requires a precise definition, such as by structure, formula, [or] chemical name, of the claimed subject matter sufficient to distinguish it from other materials" at 1405(emphasis added), and that "It does not define any structural features commonly possessed by members of the genus that distinguish from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus.." at 1406 (emphasis added). See *University of California v. Eli Lilly and Co.* 43 USPQ2d 1398 (CAFC, 1997).

Regarding the broad genus having the functional term, selective estrogen receptor modulators (SERMs), Applicant is requested to note that claims have been examined insofar as they read on the elected specie, the particular SERM, EM-652 (the instant elected species) or its pharmaceutically acceptable salts such as EM-652.HCl.

Therefore, the claims are indefinite as to the composition encompassed thereby employed in the claimed method herein.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 3-6 and 13-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Labrie (5,362,720), and Labrie et al. (WO 96/26201), and Applicant's admission regarding the prior art in the specification at 2 lines 3-4 for reasons of record in the Office Action dated November 20, 2002.

Applicant's remarks filed March 26, 2003 in Paper No. 9 with respect to this rejection made under 35 U.S.C. 103(a) of record in the previous Office Action have been fully considered but are not deemed persuasive as to the nonobviousness of the claimed invention over the prior art for the following reasons.

Applicant's assertion that the cited references neither disclose nor suggest the presently claimed combination has been considered but is not found persuasive. It has been held that it is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for same purpose in order to form a third composition that is to be used for the very same purpose; idea of combining them flows logically from their having been individually taught in prior art. *In re Kerkhoven*, 205 USPQ 1069, CCPA 1980. See MPEP 2144.06.

In the instant case, as discussed in the set forth 103(a) rejection in the previous Office Action, estrogens such as 17β-estradiol is well known in the art to be used in

estrogen therapy or Hormone Replace Therapy in menopausal women for reducing or eliminating the incidence of menopausal symptoms. Moreover, 17β-estradiol in combination with androgenic compounds or androgenic steroids is known to be capable to inhibiting breast tumor or cancer growth, and are therefore useful in methods of treating estrogen-dependent diseases, e.g., breast cancer, during estrogen therapy in menopausal women according to Labrie. Further, the particular SERM, EM-652.HCl, is known to be in methods of treating estrogen-dependent diseases. Therefore, one of ordinary skill in the art would have reasonably expected that combining an estrogen such as 17β-estradiol and the particular SERM, EM-652.HCl, or further combining an androgenic compound would be useful in reducing or eliminating the incidence of menopausal symptoms, while reducing the risk of or treating estrogen-dependent diseases such as breast cancer induced by estrogens during estrogen therapy in menopausal women for reducing or eliminating the incidence of menopausal symptoms, since each of components herein is known to be useful in the same treatment, i.e., treating estrogen-dependent diseases, absent evidence to the contrary.

Applicant argument that Labrie et al. (WO 96/26201) at page 5 lines 2-3 teaches away from using the combination herein is not found convincing. Labrie et al. (WO 96/26201) at page 5 the 3rd paragraph teaches that the compounds therein are useful in the treatment of estrogen-related diseases such as breast cancer, uterine cancer, and ovarian caner, during estrogen therapy in menopausal women. As discussed above, according to Labrie(5,362,720),17β-estradiol in combination with androgenic compounds or androgenic steroids is known to be capable to inhibiting breast tumor or

cancer growth, and are therefore useful in methods of treating estrogen-dependent diseases, e.g., breast cancer. Labrie(5,362,720) also teaches that antiestrogens are known to be administered during estrogen therapy in menopausal women (col.1-2).

One cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. In re Keller, 642 F.2d 413, 208 SPQ 871 (CCPA 1981); In re Merck & Co., Inc., 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). See MPEP 2145.

Therefore, motivation to combine the teachings of the prior art cited herein to make the present invention is seen. The claimed invention is clearly obvious in view of the prior art.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 2 is rejected under 35 U.S.C. 103(a) as being unpatentable over Labrie (5,362,720), and Labrie (5,780,460, PTO-892), and Labrie et al. (WO 96/26201), and Applicant's admission regarding the prior art in the specification at 2 lines 3-4 for reasons of record in the Office Action dated November 20, 2002.

Applicant's remarks filed March 26, 2003 in Paper No. 9 with respect to this rejection made under 35 U.S.C. 103(a) of record in the previous Office Action have

been fully considered but are not deemed persuasive as to the nonobviousness of the claimed invention over the prior art for the following reasons.

Again, Applicant's assertion that the cited references neither disclose nor suggest the presently claimed combination has been considered but is not found persuasive. As discussed above and in the previous Office Action, one of ordinary skill in the art would have reasonably expected that combining an estrogen such as 17β-estradiol and the particular SERM, EM-652.HCl, and DHEA, or further combining an androgenic compound would be useful in reducing or eliminating the incidence of menopausal symptoms, while reducing the risk of or treating estrogen-dependent diseases such as breast cancer induced by estrogens during estrogen therapy in menopausal women for reducing or eliminating the incidence of menopausal symptoms, since each of components herein is known to be useful in the same treatment, i.e., treating estrogen-dependent diseases.

Further, as discussed in the previous Office Action, Applicant's testing results in Example 1-2 and 4-5 of the specification at pages 42-53 and 60-73 have been fully considered with respect to the nonobviousness and/or unexpected results of the claimed invention but are not deemed persuasive for the following reasons. The results herein are not seen to provide clear and convincing evidence of nonobviousness or unexpected results over the cited prior art for the combination of 17β-estradiol and EM-652.HCl, or the combination of 17β-estradiol and EM-652.HCl and DHEA in the claimed

method of reducing or eliminating the incidence of menopausal symptoms. The specification provides no side-by-side comparison with the closest prior art.

Moreover, the testing herein is merely in the treatment of bone loss, a single menopausal symptom, in female rats, (see page 68-69). Thus, the evidence in the testing on is not commensurate in scope with the claimed invention and does not demonstrate criticality of a claimed broad range of menopausal symptoms herein. See MPEP § 716.02(d). Additionally, the tests herein merely employ two particular SERMs (i.e., EM-652 and EM-800), particular estrogens, and particular androgenic agents. Again, the evidence in the testing is not commensurate in scope with the claimed invention and does not demonstrate criticality of the claimed range of active agents herein in the claimed method. Further, the specification provides no evidence for treating menopausal women.

Therefore, no clear and convincing evidence of nonobviousness or unexpected results for the combination in the claimed method presented in specification herein is seen to support the nonobviousness of the instant claimed invention over the prior art.

For the above stated reasons, said claims are properly rejected under 35 U.S.C. 103(a).

In view of the rejections to the pending claims set forth above, no claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Jiang, whose telephone number is (703) 305-1008. The examiner can normally be reached on Monday-Friday from 9:00 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, Ph.D., can be reached on (703) 305-1877. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 305-1235.

S. Anna Jiang, Ph.D.
Patent Examiner, AU 1617
June 4, 2003

SREENI PADMANABHAN
PRIMARY EXAMINER 6/16/03